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DESCRIPTION

[0001] The present invention relates to a nasal delivery device for delivering a substance, in particular one of a liquid, as a suspension or solution, or a powder, such as containing a medicament, especially systemic or topical pharmaceuticals, or a vaccine, to the nasal airway of a subject.

[0002] Referring to Figure 10, the nasal airway 1 comprises the two nasal cavities separated by the nasal septum, which airway 1 includes numerous ostia, such as the paranasal sinus ostia 3 and the tubal ostia 5, and olfactory cells, and is lined by the nasal mucosa. The nasal airway 1 can communicate with the nasopharynx 7, the oral cavity 9 and the lower airway 11, with the nasal airway 1 being in selective communication with the anterior region of the nasopharynx 7 and the oral cavity 9 by opening and closing of the oropharyngeal velum 13. The velum 13, which is often referred to as the soft palate, is illustrated in solid line in the closed position, as achieved by providing a certain positive pressure in the oral cavity 9, such as achieved on exhalation through the oral cavity 9, and in dashed line in the open position.

[0003] There are many nasal conditions which require treatment. One such condition is nasal inflammation, specifically rhinitis, which can be allergic or non-allergic and is often associated with infection and prevents normal nasal function. By way of example, allergic and non-allergic inflammation of the nasal airway can typically effect between 10 and 20 % of the population, with nasal congestion of the erectile tissues of the nasal concha, lacrimation, secretion of watery mucus, sneezing and itching being the most common symptoms. As will be understood, nasal congestion impedes nasal breathing and promotes oral breathing, leading to snoring and sleep disturbance. Other nasal conditions include nasal polyps which arise from the paranasal sinuses, hypertrophic adenoids, secretory otitis media, sinus disease and reduced olfaction.

[0004] In the treatment of certain nasal conditions, the topical administration of medicaments is preferable, particularly where the nasal mucosa is the prime pathological pathway, such as in treating or relieving nasal congestion. Medicaments that are commonly topically delivered include decongestants, anti-histamines, cromoglycates, steroids and antibiotics. At present, among the known anti-inflammatory pharmaceuticals, topical steroids have been shown to have an effect on nasal congestion. Topical decongestants have also been suggested for use in relieving nasal congestion. The treatment of hypertrophic adenoids and chronic secretory otitis media using topical decongestants, steroids and anti-microbial agents, although somewhat controversial, has also been proposed. Further, the topical administration of pharmaceuticals has been used to treat or at least relieve symptoms of inflammation in the anterior region of the nasopharynx, the paranasal sinuses and the auditory tubes.

[0005] Medicaments can also be systemically delivered through the nasal pathway, the nasal pathway offering a good administration route for the systemic delivery of pharmaceuticals, such as hormones, for example, oxytocin and calcitonin, and analgetics, such as anti-migraine compositions, as the high blood flow and large surface area of the nasal mucosa

advantageously provides for rapid systemic uptake.

[0006] Nasal delivery is also expected to be advantageous for the administration of medicaments requiring a rapid onset of action, for example, analgetics, anti-emetics, insulin, anti-epileptics, sedatives and hypnotica, and also other pharmaceuticals, for example, cardio-vascular drugs. It is envisaged that nasal administration will provide for a fast onset of action, at a rate similar to that of injection and at a rate much faster than that of oral administration. Indeed, for the treatment of many acute conditions, nasal administration is advantageous over oral administration, since gastric stasis can further slow the onset of action following oral administration.

[0007] It is also expected that nasal delivery could provide an effective delivery route for the administration of proteins and peptides as produced by modern biotechnological techniques. For such substances, the metabolism in the intestines and the first-pass-effect in the liver represent significant obstacles for reliable and cost-efficient delivery.

[0008] Furthermore, it is expected that nasal delivery using the nasal delivery technique of the present invention will prove effective in the treatment of many common neurological diseases, such as Alzheimer's, Parkinson's, psychiatric diseases and intracerebral infections, where not possible using existing techniques. The nasal delivery technique of the present invention allows for delivery to the olfactory region, which region is located in the superior region of the nasal cavities and represents the only region where it is possible to circumvent the blood-to-brain barrier (BBB) and enable communication with the cerebrospinal fluid (CSF) and the brain.

[0009] Also, it is expected that the nasal delivery technique of the present invention will allow for the effective delivery of vaccines.

[0010] Aside from the delivery of medicaments, the irrigation of the nasal mucosa with liquids, in particular saline solutions, is commonly practised to remove particles and secretions, as well as to improve the mucociliary activity of the nasal mucosa. These solutions can be used in combination with active pharmaceuticals.

[0011] For any kind of drug delivery, accurate and reliable dosing is essential, but it is of particular importance in relation to the administration of potent drugs which have a narrow therapeutic window, drugs with potentially serious adverse effects and drugs for the treatment of serious and life-threatening conditions. For some conditions, it is essential to individualize the dosage to the particular situation, for example, in the case of diabetes mellitus. For diabetes, and, indeed, for many other conditions, the dosage of the pharmaceutical is preferably based on actual real-time measurements. Currently, blood samples are most frequently used, but the analysis of molecules in the exhalation breath of subjects has been proposed as an alternative to blood analysis for several conditions. Breath analysis is currently used for the diagnosis of conditions such as helicobacter pylori infections which cause gastric ulcers.

[0012] WO-A-2000/051672 discloses a delivery device for delivering a substance, in particular a medicament, in a bi-directional flow through the nasal cavities, that is, an air flow which passes into one nostril, around the posterior margin of the nasal septum and in the opposite direction out of the other nostril. This bi-directional air flow advantageously acts to stimulate the sensory nerves in the nasal mucosa, thereby conditioning the subject for the delivery and providing a more comfortable delivery situation.

[0013] US-A-2011/0088690 discloses a nasal delivery device which includes a manually-actuatabie substance supply unit.

[0014] US-A-6648848 discloses a device for applying a powdered or particulate substance to a mucous membrane in a nostril which comprises a tubular body similar to a drinking straw.

[0015] US-A-2011/0259329 discloses a breath-actuated delivery device which includes a mouthpiece through which a subject in use exhales, an air channel which is in fluid communication with the mouthpiece, and a flexible diaphragm which is disposed in the air channel.

[0016] US-A-2008/0163874 discloses a breath-actuated nasal delivery device which comprises a mouthpiece through which a user in use exhales to actuate the delivery device, a nosepiece for fitting to a nostril of the user through which a substance is in use delivered, a substance supply unit which is actuatable to deliver a dose of a substance through the nosepiece, a loading unit which is operable to load the substance supply unit with an actuation force, and a release mechanism for enabling actuation of the substance supply unit in response to exhalation by the user through the mouthpiece.

[0017] It is an aim of the present invention to provide nasal delivery devices for delivering substances to a nasal cavity of subject, and in particular relatively-simple mechanically-actuatable delivery devices.

[0018] In one aspect the present invention provides a nasal delivery device for delivering substance to a nasal airway of a subject according to claim 1.

[0019] Preferred embodiments of the present invention will now be described hereinbelow by way of example only with reference to the accompanying drawings, in which:

Figures 1(a) and (b) illustrate a perspective view of a nasal delivery device in accordance with a first embodiment of the present invention;

Figure 2 illustrates an exploded perspective view of the delivery device of Figure 1;

Figure 3 illustrates a vertical sectional view of the delivery device of Figure 1, in the at rest, non-actuated configuration;

Figure 4 illustrates a vertical sectional view of the delivery device of Figure 1, in the actuated

configuration;

Figure 5 illustrates an exploded, fragmentary vertical sectional view of the delivery device of Figure 1, in the actuated configuration;

Figures 6(a) to (c) illustrate the opening of the sealing member of the valve assembly by operation of the delivery unit of the delivery device of Figure 1;

Figure 7 illustrates plots of the flow rates at the nosepiece and the mouthpiece and the pressure at the mouthpiece for one exemplary device;

Figures 8(a) and (b) illustrate fragmentary vertical sectional views in the at rest, non-actuated and actuated configurations of a nasal delivery device in accordance with a second embodiment of the present invention;

Figures 9(a) and (b) illustrate fragmentary vertical sectional views in the at rest, non-actuated and actuated configurations of a nasal delivery device in accordance with a third embodiment of the present invention; and

Figure 10 schematically illustrates the anatomy of the upper respiratory tract of a human subject.

Figures 1 to 7 illustrate a manually-actuated nasal delivery device in accordance with a first embodiment of the present invention.

[0020] The delivery device comprises a housing 115, a nosepiece 117 for fitting in a nasal cavity of a subject, a mouthpiece 119 into which the subject in use exhales, such as to enable delivery of an air flow into and through the nasal airway of the subject on exhalation by the subject through the mouthpiece 119, and a delivery unit 120, which is manually actuatable to deliver substance to the nasal cavity of the subject.

[0021] The housing 115 comprises a body member 121, in this embodiment of substantially elongate, tubular section which includes an aperture 123 at one end thereof, through which projects an actuating part of the delivery unit 120, in this embodiment as defined by the base of a substance-containing chamber 173 of a substance-supply unit 169.

[0022] In this embodiment the body member 121 comprises two body sections 121a, b which are fixed together.

[0023] In this embodiment the body sections 121a, b include inter-engaging lugs 124 and detents 125, here of snap-fit type, and sealing elements 126, which act to close the air flow paths at the junctions of the body sections 121a, b.

[0024] In this embodiment the sealing elements 126 are adhesively bonded, but could alternatively be mechanically bonded, such as by welding.

[0025] In an alternative embodiment the sealing elements 126 could be omitted.

[0026] The housing 115 further comprises a valve assembly 127 which is fluidly connected to the nosepiece 117 and the mouthpiece 119, and operable between closed and open configurations, as illustrated in Figures 3 and 4, such as to provide for an air flow, in this embodiment in the form of a burst of air, through the nosepiece 117 simultaneously with actuation of the delivery unit 120, as will be described in more detail hereinbelow.

[0027] The valve assembly 127 comprises a main, body element 128 which includes a valve seat 129 defining a valve opening 130, and a valve element 131 which is movably disposed to the body element 128 between closed and open positions, as illustrated in Figures 3 and 4.

[0028] As particularly illustrated in Figure 3, the body element 128 comprises a pivot 135, in this embodiment to one, lower side of the valve seat 129, to which one end 145 of the valve element 131 is pivoted, and a sliding surface 137, in this embodiment to the other, upper side of the valve seat 129, against which the other end 147 of the valve element 131 is slideable.

[0029] The valve element 131 comprises an elongate arm 141, in this embodiment a flexible arm, one end 145, in this embodiment the lower end, of which is pivoted to the pivot 135 of the body element 128, and the other, upper end 147 of which slideably engages the sliding surface 137 of the body element 128, and a sealing member 149 which is supported by the arm 141.

[0030] In this embodiment the arm 141 comprises a first, here lower, arm section 151, which is biased, here inwardly, such that, when the valve element 131 is in the closed, rest position, the lower arm section 151 is inclined inwardly relative to the longitudinal axis of the housing 115 and engageable by the substance-supply unit 169 when manually actuated to move the valve element 131 to the open position, as will be described in more detail hereinbelow.

[0031] In this embodiment the arm 141 further comprises a second, here upper, arm section 153, which engages the sliding surface 137 of the body element 128 and acts to bias the valve element 131 to the closed position.

[0032] In this embodiment the sealing member 149 comprises a seal 161, in this embodiment a flexible or resilient element, which acts to close the valve opening 130 as defined by the valve seat 129 when the valve element 131 is in the closed position, and a support 163 which supports a central region of the seal 161.

[0033] With this configuration, and referring to Figures 6(a) to (c), where the seal 161 is centrally supported, when the valve element 131 is moved to the open position, the support 163 biases the central region of the seal 161, as illustrated in Figure 6(b), causing the seal 161 to bulge outwardly in this central region and thus provide that the seal 161 engages the valve seat 129 only at the peripheral edge of the seal 161, until the point is reached when the seal 161 is suddenly and explosively released from the valve seat 129, as illustrated in Figure 6(c).

[0034] This mode of release is believed to be particularly effective in the present application where it is desired to achieve a sudden, initial burst of air flow, in that substantially the entire sealing surface of the seal 161 is released in one instant, which compares to an alternative mode of a peeling-type release, where a smaller section of a sealing surface is released, followed by the remainder of the sealing surface, which tends to provide a smaller initial burst pressure.

[0035] In this embodiment the delivery unit 120 comprises an outlet unit 167 for delivering substance into the nasal airway of the subject, and a substance-supply unit 169 for delivering substance to the outlet unit 167.

[0036] In this embodiment the valve assembly 127 provides for a pre-actuation efficiency of less than 5 L/min when a user is developing an exhalation pressure of 3 kPa, preferably less than 5 L/min when a user is developing an exhalation pressure of 10 kPa, more preferably less than 1 L/min when a user is developing an exhalation pressure of 3 kPa, still more preferably less than 1 L/min when a user is developing an exhalation pressure of 10 kPa, yet more preferably substantially no flow when a user is developing an exhalation pressure of 3 kPa, and still yet more preferably substantially no flow when a user is developing an exhalation pressure of 10 kPa; the pre-actuation efficiency being a measure of the volume of air which escapes from the device prior to actuation as a fraction of the volume of air delivered into the mouthpiece 119.

[0037] In this embodiment the delivery device is configured to provide a post-actuation efficiency of at least 80% at a flow rate of 50 L/min and an exhalation pressure of 3 kPa, preferably at least 85% at a flow rate of 50 L/min and an exhalation pressure of 3 kPa, more preferably at least 88% at a flow rate of 50 L/min and an exhalation pressure of 3 kPa, and yet more preferably at least 90% at a flow rate of 50 L/min and an exhalation pressure of 3 kPa; the post-actuation efficiency being a measure of the volume of air delivered from the nosepiece 117 as a fraction of the volume of air delivered into the mouthpiece 119.

[0038] Figure 7 illustrates, for one exemplary device, plots of the flow rates at the nosepiece 117 and the mouthpiece 119 and the pressure at the mouthpiece 119.

[0039] In this embodiment the pre-actuation efficiency of 1 L/min at a pre-actuation pressure of 5 kPa.

[0040] In this embodiment the post-actuation efficiency is 88% at a flow rate of 57.1 L/min.

[0041] In this embodiment, the valve element 131 provides for a burst of air flow on opening thereof, having a first, initial burst: phase followed by a second, extended burst phase, wherein the peak flow rate in the initial burst phase has a higher flow rate than the average flow rate in the extended burst phase, and the extended burst phase is of substantially greater duration than the initial burst phase.

[0042] In this embodiment the peak flow rate in the initial burst phase is at least 10%, preferably at least 15%, and more preferably at least 20%, greater than that of the average flow rate of the extended burst phase in a period corresponding to ten times the duration of the period in which substance is delivered from the nosepiece 117 by the delivery unit 120.

[0043] In this embodiment the delivery unit 120 provides a spray which commences 54 ms after opening of the sealing member 149 and terminates 134 ms after opening of the sealing member 149.

[0044] In one embodiment the delivery unit 120 provides for delivery of substance subsequent to opening of the sealing member 149.

[0045] In one embodiment the delivery unit 120 provides for delivery of substance in a period less than about 250 ms from opening of the sealing member 149, preferably less than about 200 ms from opening of the sealing member 149, more preferably less than about 150 ms from opening of the sealing member 149, and still more preferably more preferably less than about 100 ms from opening of the sealing member 149.

[0046] In one embodiment the delivery unit 120 provides for delivery of substance commencing less than about 150 ms subsequent to opening of the sealing member 149, preferably less than about 100 ms subsequent to opening of the sealing member 149, still more preferably less than about 50 ms subsequent to opening of the sealing member 149, yet more preferably less than more than about 25 ms subsequent to opening of the sealing member 149, still more preferably less than about 15 ms subsequent to opening of the sealing member 149.

[0047] In this embodiment the outlet unit 167 comprises a nozzle 171 for delivering substance to the nasal airway of the subject. In this embodiment the nozzle 171 is configured to provide an aerosol spray. In an alternative embodiment, for the delivery of a liquid, the nozzle 171 could be configured to deliver a liquid jet as a column of liquid.

[0048] In a preferred embodiment the distal end of the outlet unit 167 is configured to extend at least about 2 cm, preferably at least about 3 cm, and more preferably from about 2 cm to about 3 cm, into the nasal cavity of the subject.

[0049] In this embodiment the substance supply unit 169 is a pump unit, which comprises a substance-containing chamber 173 which contains substance and extends from the aperture 123 in the housing 115 as the actuating part of the substance-supply unit 169, and a mechanical delivery pump 175 which is actuatable, here by depression of the substance-containing chamber 173, typically by a finger or thumb of the subject, to deliver a metered dose of substance from the substance-containing chamber 173 to the outlet unit 167 and from the nozzle 171 thereof, here as an aerosol spray.

[0050] In this embodiment the substance-containing chamber 173, when depressed to actuate

the substance supply unit 169, engages the lower arm section 151 of the arm 141 of the valve element 131, such as simultaneously to provide for actuation of the substance-supply unit 169 and opening of the seal 161 of the valve element 131, whereby substance, here in the form of a spray, and an air flow, here as a burst of air, are simultaneously delivered to the nasal cavity of the subject.

[0051] In this embodiment the mechanical delivery pump 175 is a liquid delivery pump for delivering a metered dose of substance, but in an alternative embodiment the mechanical delivery pump 175 could be a powder delivery pump, which delivers metered doses of a powdered substance on actuation thereof.

[0052] In this embodiment the substance-supply unit 169 is a multi-dose unit for delivering a plurality of metered doses of substance in successive delivery operations.

[0053] In an alternative embodiment the substance-supply unit 169 could be a single-dose unit for delivering a single metered dose of substance or a duo-dose unit for delivering two metered doses of substance in two successive delivery operations.

[0054] In another alternative embodiment the substance-supply unit 169 could comprise a dry powder delivery unit which delivers metered doses of a substance, as a dry powder, on actuation thereof.

[0055] In yet another alternative embodiment the substance-supply unit 169 could comprise a nebulizer which delivers metered doses of a substance, as an aerosol spray, on actuation thereof.

[0056] In still another alternative embodiment the substance-supply unit 169 could comprise an aerosol canister for delivering metered volumes of a propellant, preferably a hydrofluoroalkane (HFA) propellant or the like, containing substance, either as a suspension or solution.

[0057] In this embodiment the housing 115 further comprises a sealing member 181, here an annular seal, in the form of an O-ring, which slideably receives the substance-containing chamber 173 of the substance-supply unit 169, such as to prevent the escape of the delivered air flow from the aperture 123 in the housing 115.

[0058] In one embodiment the sealing member 181 could be omitted.

[0059] Figures 8(a) and (b) illustrate a nasal delivery device in accordance with a second embodiment of the present invention.

[0060] The delivery device of this embodiment is substantially the same as the delivery device of the first-described embodiment, and thus, in order to avoid unnecessary duplication of description, only the differences will be described in detail, with like parts being designated by

like reference signs.

[0061] The delivery device of this embodiment differs from that of the first-described embodiment principally in that the sealing member 149 is configured such that the support 163 extends across substantially the entire width of the valve opening 130. In this way, the seal 161 is not able to bulge in the manner of the above-described embodiment, and is instead opened by a peeling action. Figure 8(a) illustrates the valve assembly 127 in the at rest, non-actuated configuration. Figure 8(b) illustrates the valve assembly 127 in the actuated configuration.

[0062] Figures 9(a) and (b) illustrate a nasal delivery device in accordance with a third embodiment of the present invention.

[0063] The delivery device of this embodiment is very similar to the delivery device of the first-described embodiment, and thus, in order to avoid unnecessary duplication of description, only the differences will be described in detail, with like parts being designated by like reference signs.

[0064] The delivery device of this embodiment differs from that of the first-described embodiment principally in that the seal 161 is not supported by the arm 141, but is instead a separate element, which is displaced by movement of the arm 141, as caused by manual actuation of the substance-supply unit 169. Figure 9(a) illustrates the valve assembly 127 in the at rest, non-actuated configuration. Figure 9(b) illustrates the valve assembly 127 in the actuated configuration.

[0065] In this embodiment the seal 161 comprises a flexible element, here in the form of a flap, and in one embodiment a resilient element, which is engaged by an engagement element 185 on the arm 141.

[0066] In this embodiment the engagement element 185 comprises a projection which acts to cause the seal 161 to bulge in the manner of the first-described embodiment.

[0067] In an alternative embodiment the engagement element 185 could extend across substantially the width of the valve opening 130, causing the seal 161 to be moved from the valve seat 129 with a peeling action in a similar manner to the second-described embodiment.

[0068] Finally, it will be understood that the present invention has been described in its preferred embodiments and can be modified in many different ways without departing from the scope of the invention as defined by the appended claims.

REFERENCES CITED IN THE DESCRIPTION

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Patentkrav

1. Nasal indgivelsesindretning til indgivelse af substans til en nasal luftvej af et individ, omfattende:

et næsestykke (117) til tilpasning til en næsehule af et individ;

et mundstykke (119) i hvilket individet under brug udånder;

en indgivelsesenhed (120), der omfatter en aktiveringsdel (173), der er manuelt forskydelig til at aktivere indgivelsesenheden (120) til at indgive substans fra næsestykket (119); og

en ventilanordning (127), der er fluidforbundet til næsestykket (117) og mundstykket (119), hvor ventilanordningen (127) omfatter et kropselement (128) og et ventilelement (131), som er bevægeligt anbragt i forhold til kropselementet (128) mellem lukkede og åbne konfigurationer ved manuel forskydning af aktiveringsdelen (173) af indgivelsesenheden (120) for at tilvejebringe en luftstrøm igennem næsestykket (117) samtidigt med indgivelse af substans;

kendetegnet ved, at:

kropselementet (128) inkluderer et ventilsæde (129) der definerer en ventilåbning (130), og ventilelementet (131) omfatter en tætning (161) der fungerer til at lukke ventilåbningen (130), når ventilelementet (131) er i den lukkede position og en bærer (163) der bærer et centralt område af tætningen (161) for således at muliggøre et perifert område af tætningen (161) at indgribe ventilsædet (129) og det centrale område, som skal forskydes i forhold til det perifere område, for derved at muliggøre for pludselig frigivelse af tætningen (161), og hvorved ventilanordningen (127), ved åbning af ventilelementet (131), tilvejebringer en sprængning af luftstrøm, som har en første, indledende sprængningsfase efterfulgt af en anden udvidet sprængningsfase, hvor topstrømningshastigheden i den første sprængningsfase er mindst 10 % større end den af den gennemsnitlige strømningshastighed af den anden sprængningsfase i en periode svarende til ti gange varigheden af perioden i hvilken substans indgives fra indgivelsesenheden (120).

2. Indgivelsesindretningen ifølge krav 1, hvor topstrømningshastigheden i den første sprængningsfase er mindst 15 % større end den af den gennemsnitlige strømningshastighed af den anden sprængningsfase i en periode svarende til ti gange varigheden af perioden i hvilken substans indgives fra indgivelsesenheden (120).

3. Indgivelsesindretningen ifølge krav 1, hvor topstrømningshastigheden i den første sprængningsfase er mindst 20 % større end den af den gennemsnitlige strømningshastighed af den anden sprængningsfase i en periode svarende til ti gange varigheden af perioden i hvilken substans indgives fra indgivelsesenheden (120).

4. Indgivelsesindretningen ifølge et hvilket som helst af kravene 1 til 3, yderligere omfattende:

et hus (115) der inkluderer en åbning (123) igennem hvilken aktiveringsdelen (173) af indgivelsesenheden (120) strækker sig, eventuelt hvor huset (115) yderligere omfatter et tætningselement (181) der forskydeligt modtager aktiveringsdelen (173) for at forhindre luftstrøm fra åbningen (123) i huset (115).

5. Indgivelsesindretningen ifølge et hvilket som helst af kravene 1 til 4, hvor ventilanordningen (127) er konfigureret til at tilvejebringe en præaktiveringsstrømning på mindre end 5 L/min når en bruger udvikler et udåndingstryk på 3 kPa, eventuelt hvor ventilanordningen (127) er konfigureret til at tilvejebringe en præaktiveringsstrømning på mindre end 5 L/min når en bruger udvikler et udåndingstryk på 10 kPa.

6. Indgivelsesindretningen ifølge et hvilket som helst af kravene 1 til 4, hvor ventilanordningen (127) er konfigureret til at tilvejebringe en præaktiveringsstrømning på mindre end 1 L/min når en bruger udvikler et udåndingstryk på 3 kPa, eventuelt hvor ventilanordningen (127) er konfigureret til at tilvejebringe en præaktiveringsstrømning på mindre end 1 L/min når en bruger udvikler et udåndingstryk på 10 kPa.

7. Indgivelsesindretningen ifølge et hvilket som helst af kravene 1 til 6, hvor indgivelsesindretningen er konfigureret til at tilvejebringe mindst 80 % af luften som indgivet i mundstykket (119) til næsestykket (117) når indgivet ved en strømningshastighed på 50 L/min og et udåndingstryk på 3 kPa, eventuelt hvor indgivelsesindretningen er konfigureret til at tilvejebringe mindst 88 % af luften som indgivet i mundstykket (119) til næsestykket (117) når indgivet ved en strømningshastighed på 50 L/min og et udåndingstryk på 3 kPa, eventuelt hvor indgivelsesindretningen er konfigureret til at tilvejebringe mindst 90 % af luften som indgivet i mundstykket (119) til næsestykket (117) når indgivet ved en strømningshastighed på 50 L/min og et udåndingstryk på 3 kPa.

8. Indgivelsesindretningen ifølge et hvilket som helst af kravene 1 til 7, hvor ventilelementet (131) omfatter et tætningselement (149) og indgivelsesenheden (120) er konfigureret til at tilvejebringe indgivelse af substans efter åbning af tætningselementet (149) af ventilelementet (131).

9. Indgivelsesindretningen ifølge krav 8, hvor indgivelsesenheden (120) er konfigureret til at tilvejebringe indgivelse af substans i en periode mindre end 250 ms fra åbning af tætningselementet (149) af ventilelementet (131), eventuelt i en periode mindre end 200 ms fra åbning af tætningselementet (149) af ventilelementet (131), eventuelt i en periode mindre end 150 ms fra åbning af tætningselementet (149) af ventilelementet (131), eventuelt i en periode mindre end 100 ms fra åbning af tætningselementet (149) af ventilelementet (131).

10. Indgivelsesindretningen ifølge krav 8 eller 9, hvor indgivelsesenheden (120) er konfigureret til at tilvejebringe indgivelse af substans begyndende mindre end 150 ms efter åbning af tætningselementet (149) af ventilelementet (131), eventuelt mindre end 100 ms efter åbning af tætningselementet (149) af ventilelementet (131), eventuelt mindre end 50 ms efter åbning af tætningselementet (149) af ventilelementet (131), eventuelt mindre end 25 ms efter åbning af tætningselementet (149) af ventilelementet (131), eventuelt mindre end 15 ms efter åbning af tætningselementet (149) af ventilelementet (131).

11. Indgivelsesindretningen ifølge et hvilket som helst af kravene 1 til 10, hvor indgivelsesenheden (120) omfatter en udløbsenhed (167) fra hvilken substans er indgivet igennem næsestykket (117) og en substansforsyningsenhed (169), som er aktiverbar til at indgive substans til udløbsenheden (167), eventuelt hvor udløbsenheden (167) omfatter en sprøjtedyse (171).

12. Indgivelsesindretningen ifølge krav 11, hvor aktiveringsdelen (173) af indgivelsesenheden (120) omfatter et substansindeholdende kammer (173) af substansforsyningsenheden (169).

13. Indgivelsesindretningen ifølge krav 12, hvor substansforsyningsenheden (169) omfatter en mekanisk indgivelsespumpe (175), som er aktiverbar ved nedtrykning af det substansindeholdende kammer (173).

DRAWINGS

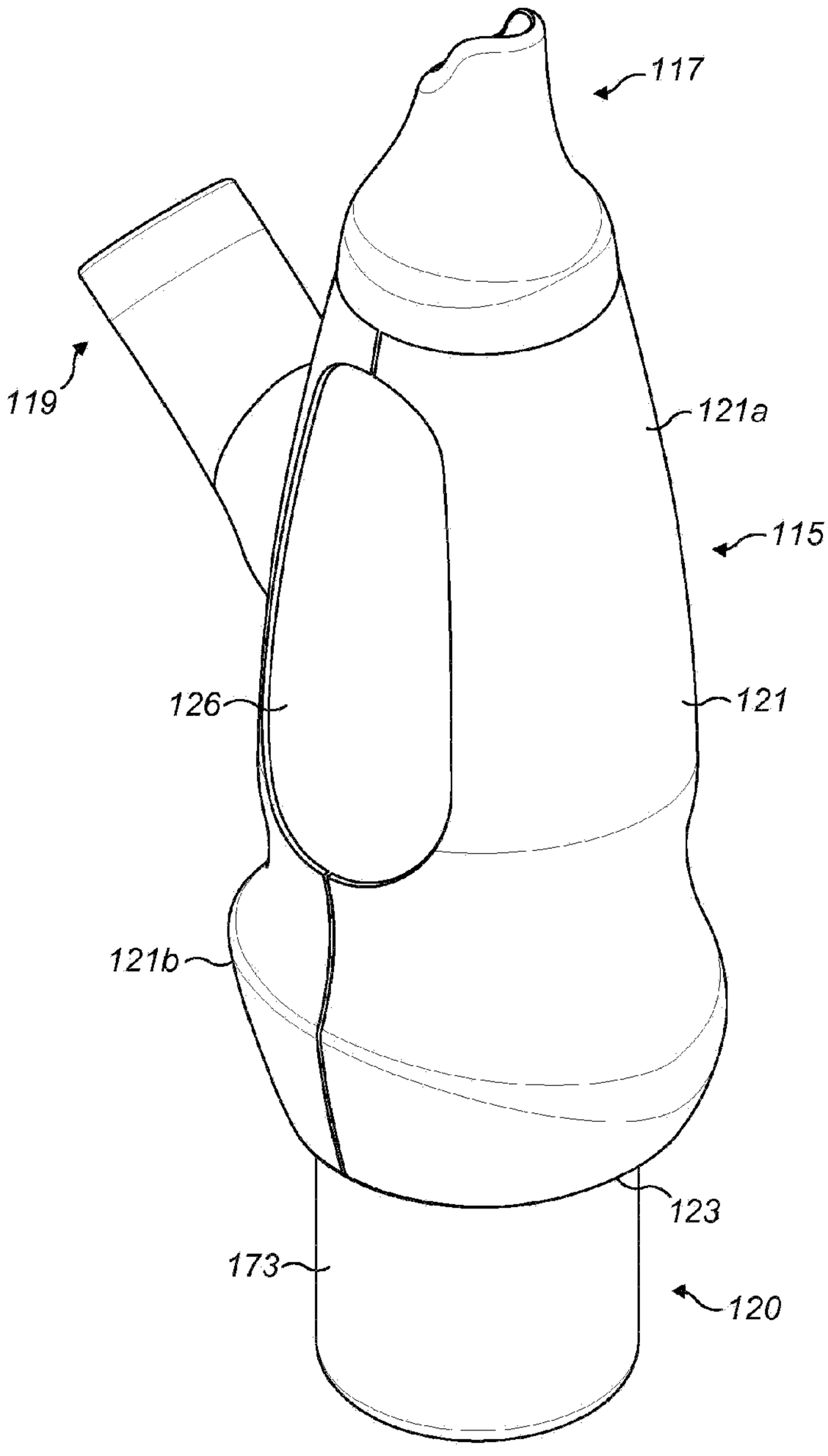


FIG. 1(a)

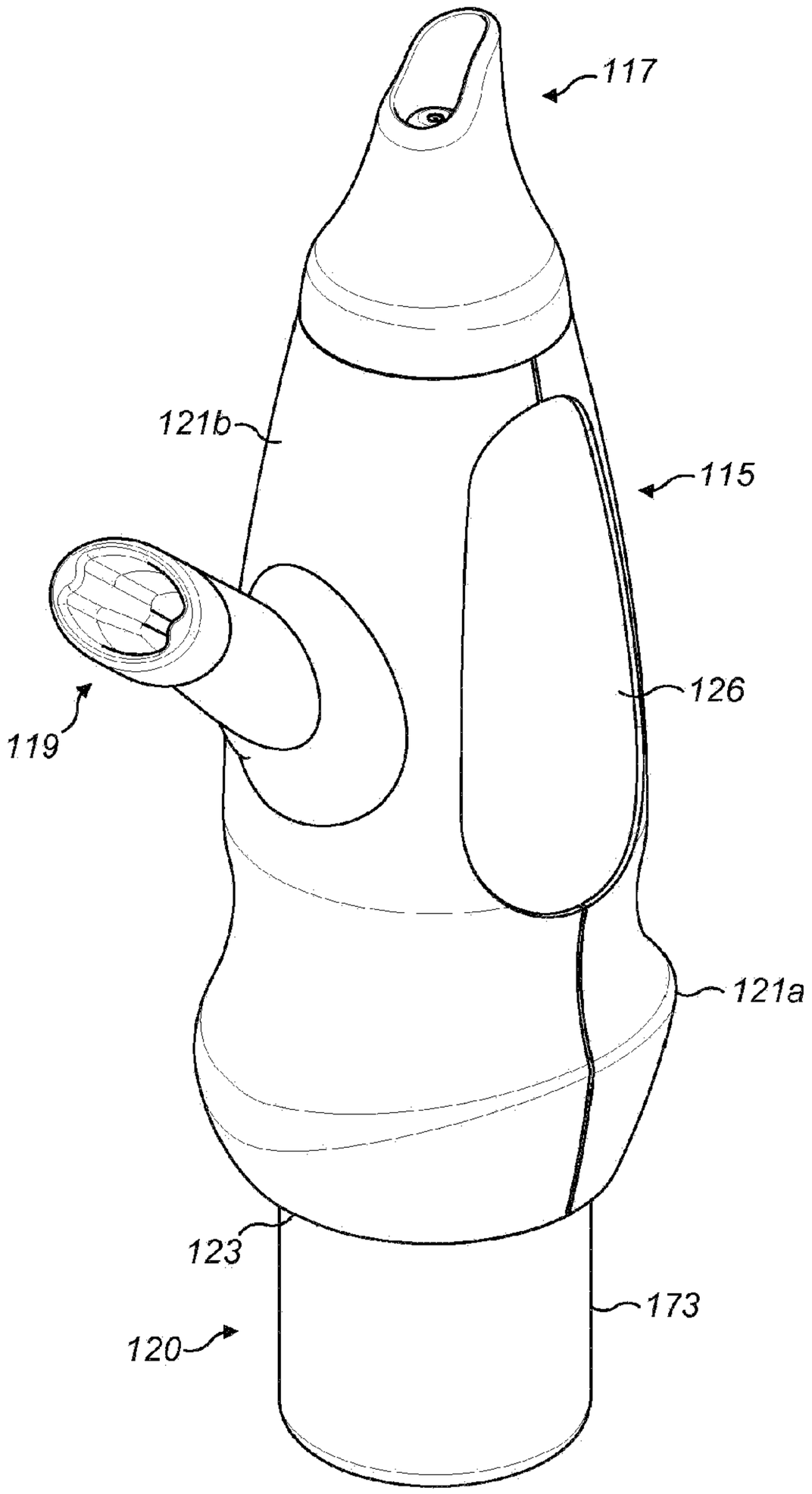


FIG. 1(b)

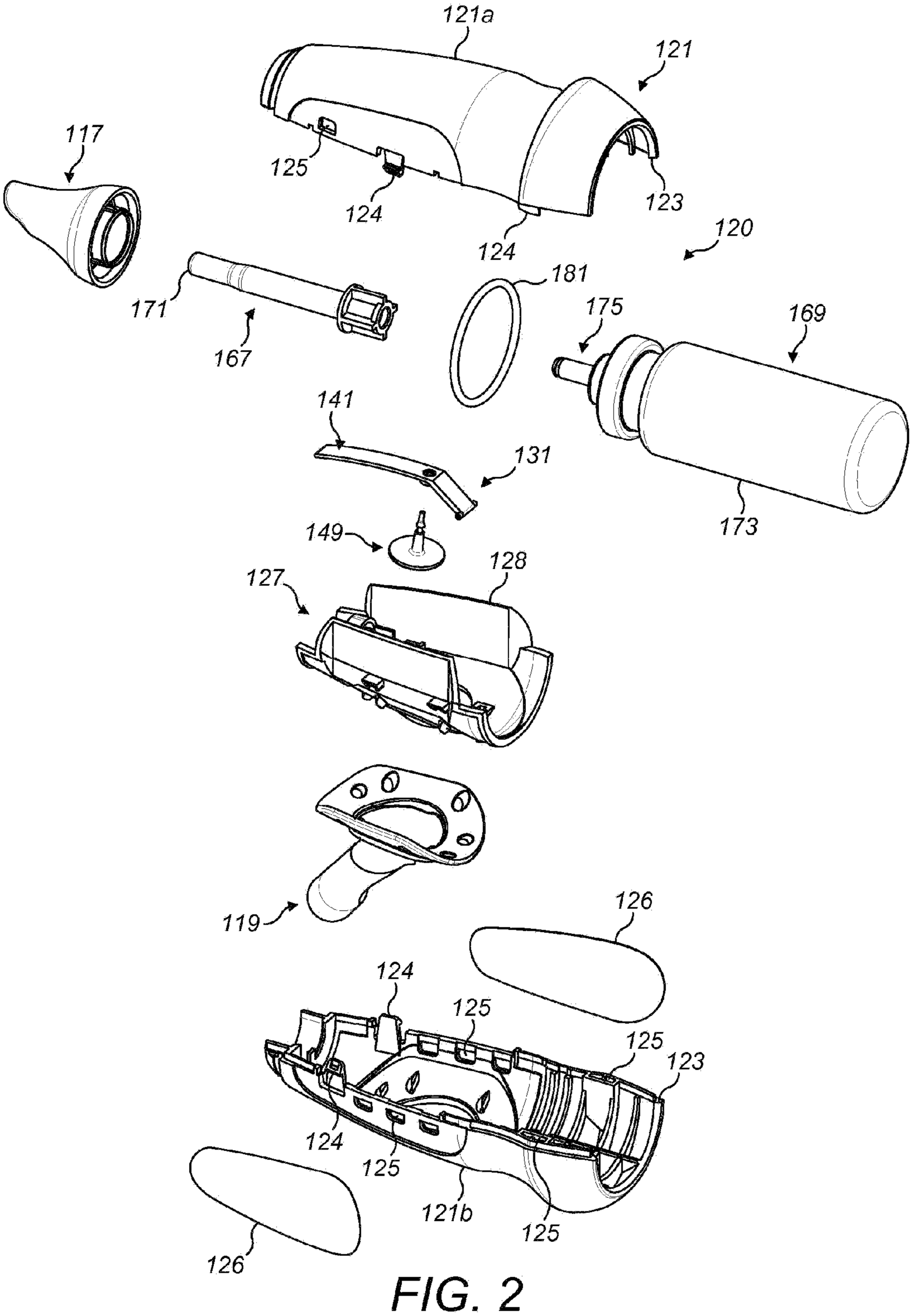

121a
121
117
125
124
123
124
120
171
181
175
169
167
141
131
173
149
128
127
119
126
124
125
125
123
124
125
121b
125
126

FIG. 2

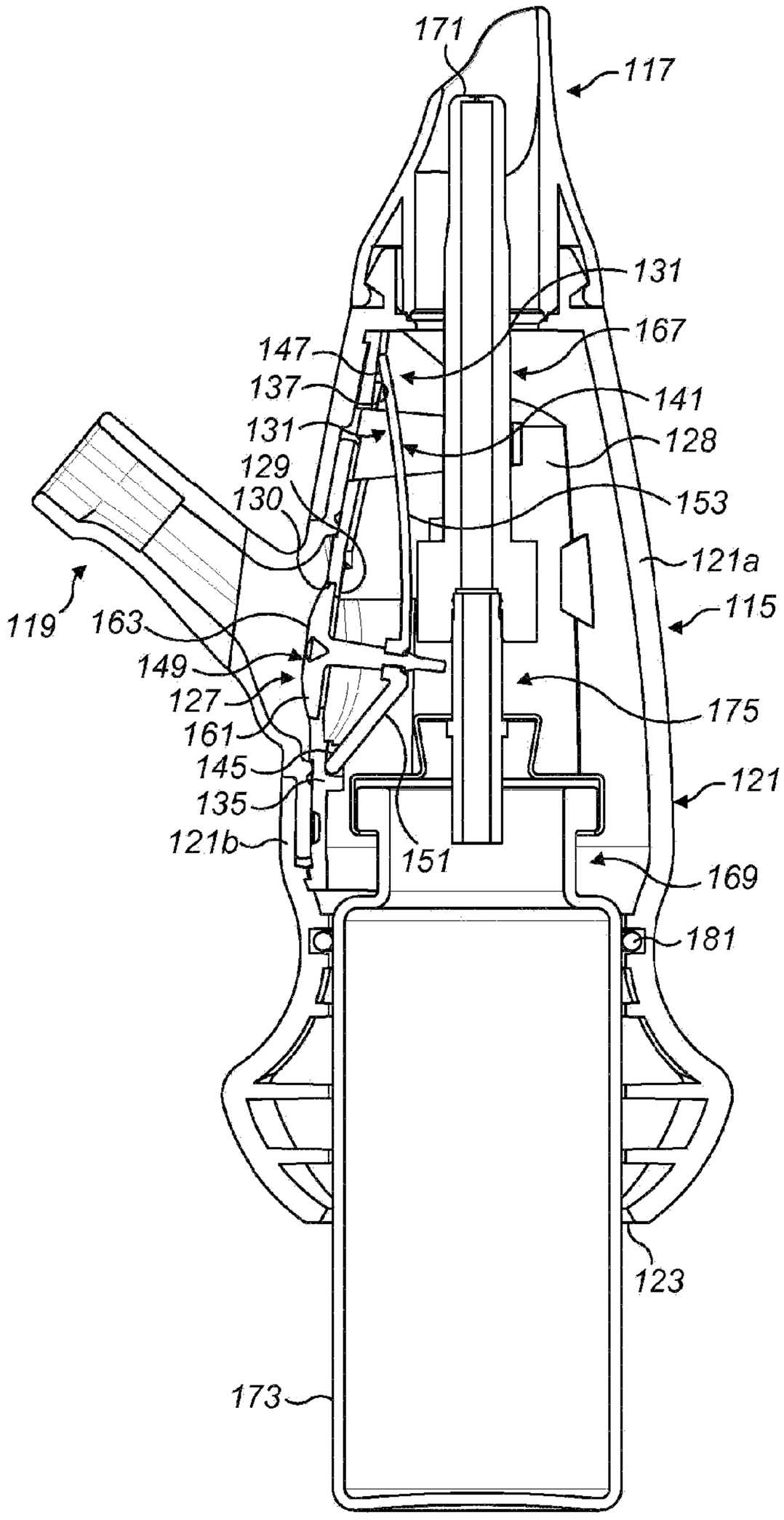

171
117
131
167
147
137
141
131
128
129
130
153
121a
119
163
115
149
127
175
161
145
121
135
121b
151
169
181
123
173

FIG. 3

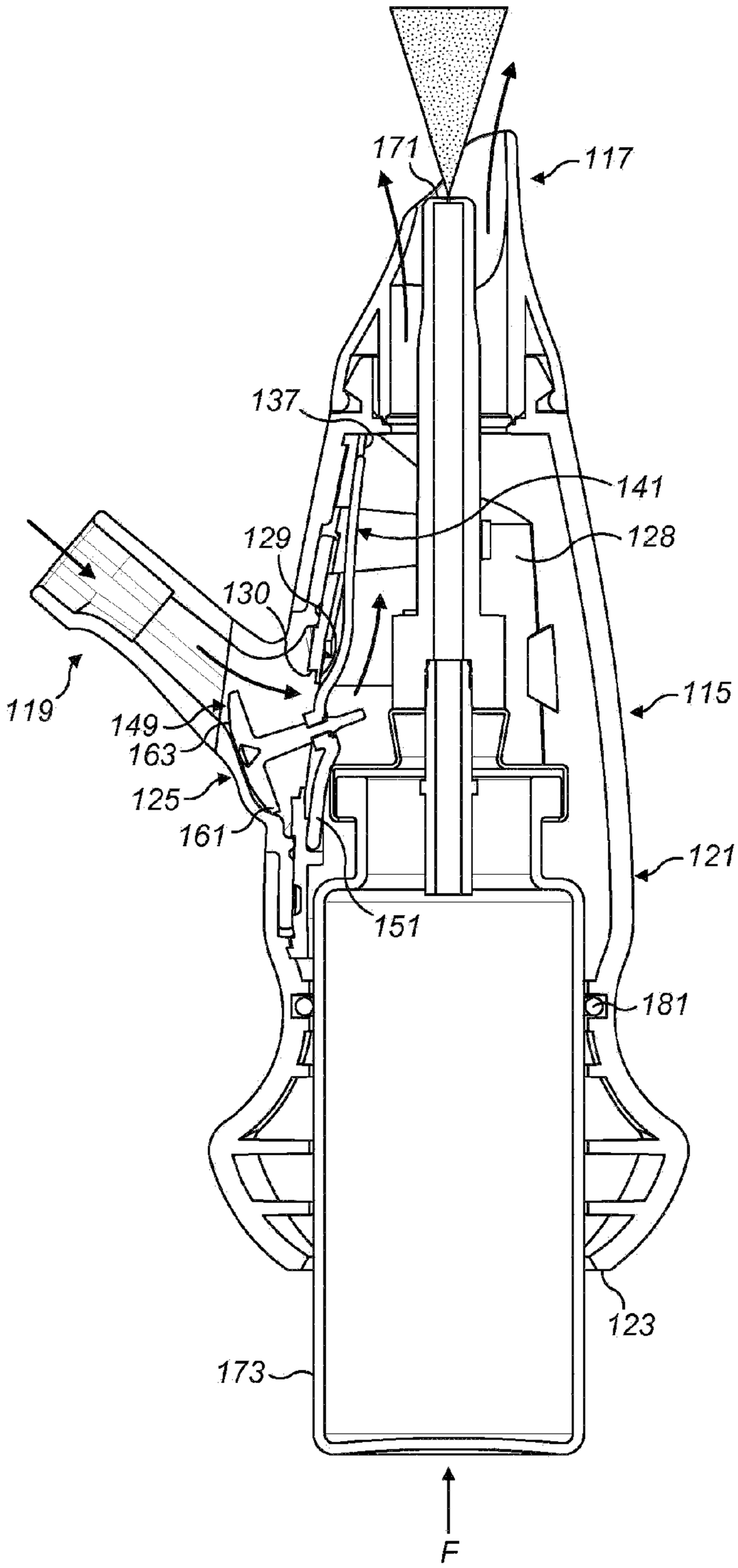

171
117
137
141
129
128
130
115
119
149
163
125
161
121
151
181
123
173
F

FIG. 4

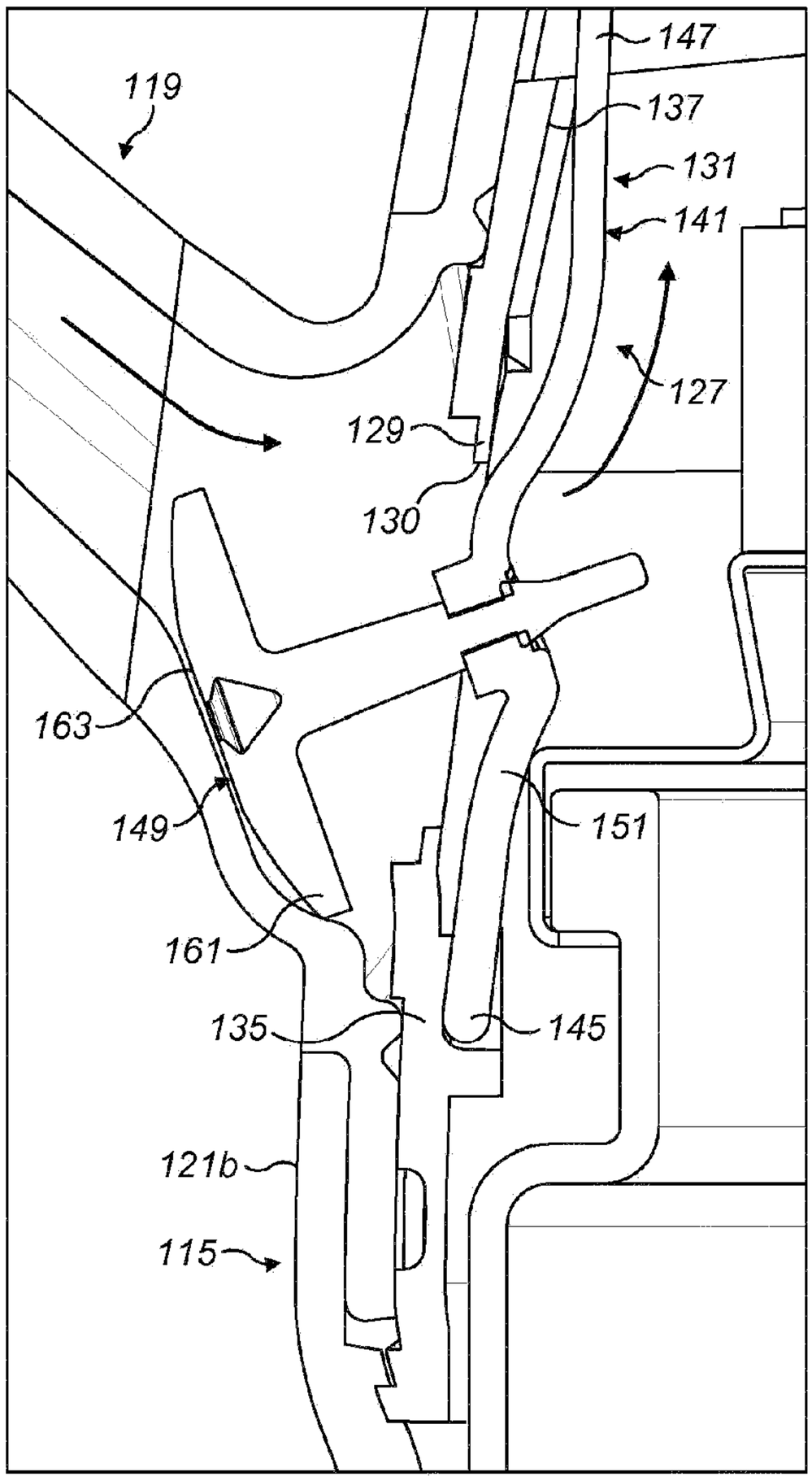


FIG. 5

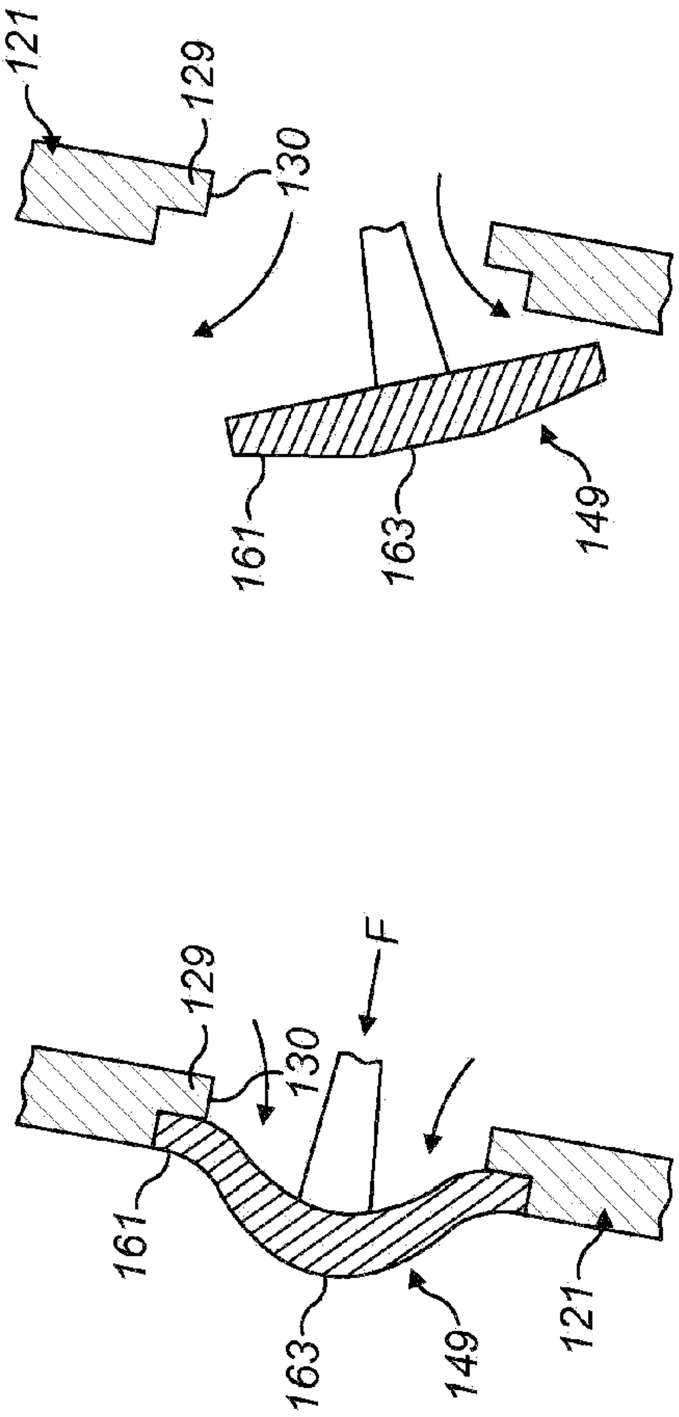


FIG. 6(c)

FIG. 6(b)

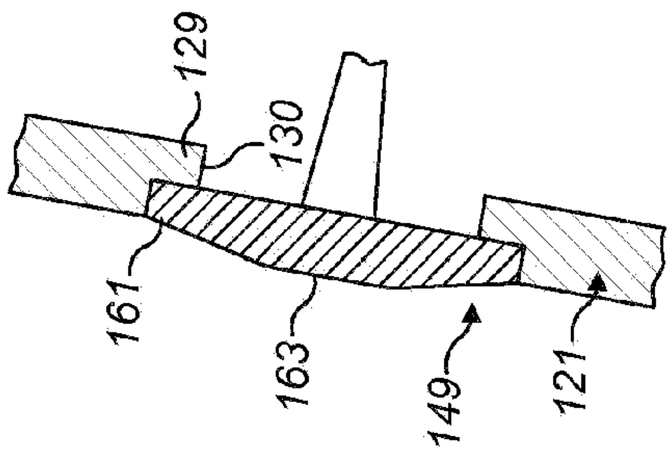


FIG. 6(a)

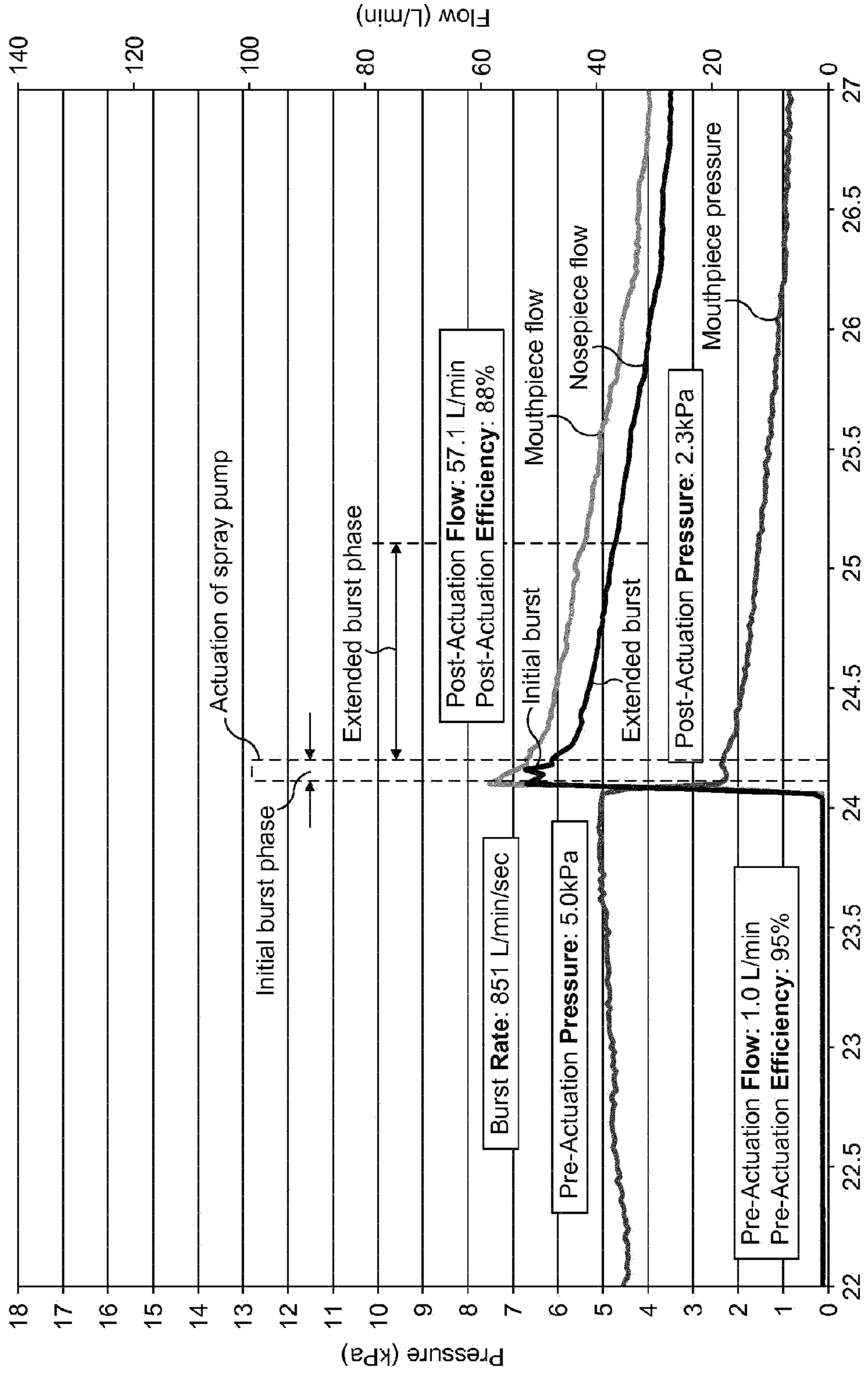

Pressure (kPa)
Flow (L/min)
Time (sec)
Actuation of spray pump
Initial burst phase
Extended burst phase
Initial burst
Extended burst
Post-Actuation Flow: 57.1 L/min
Post-Actuation Efficiency: 88%
Burst Rate: 851 L/min/sec
Pre-Actuation Pressure: 5.0kPa
Post-Actuation Pressure: 2.3kPa
Pre-Actuation Flow: 1.0 L/min
Pre-Actuation Efficiency: 95%
Mouthpiece flow
Nosepiece flow
Mouthpiece pressure

FIG. 7

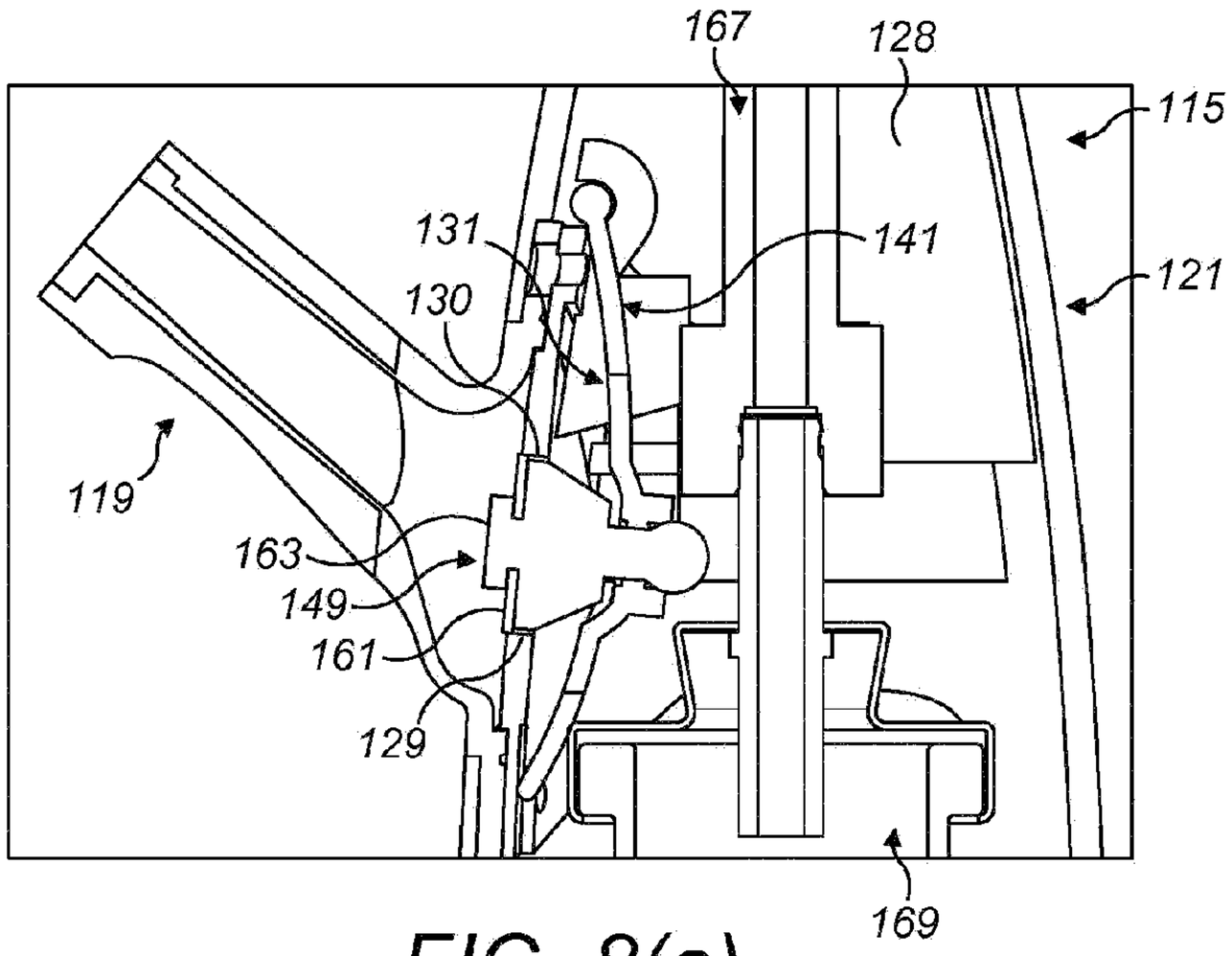
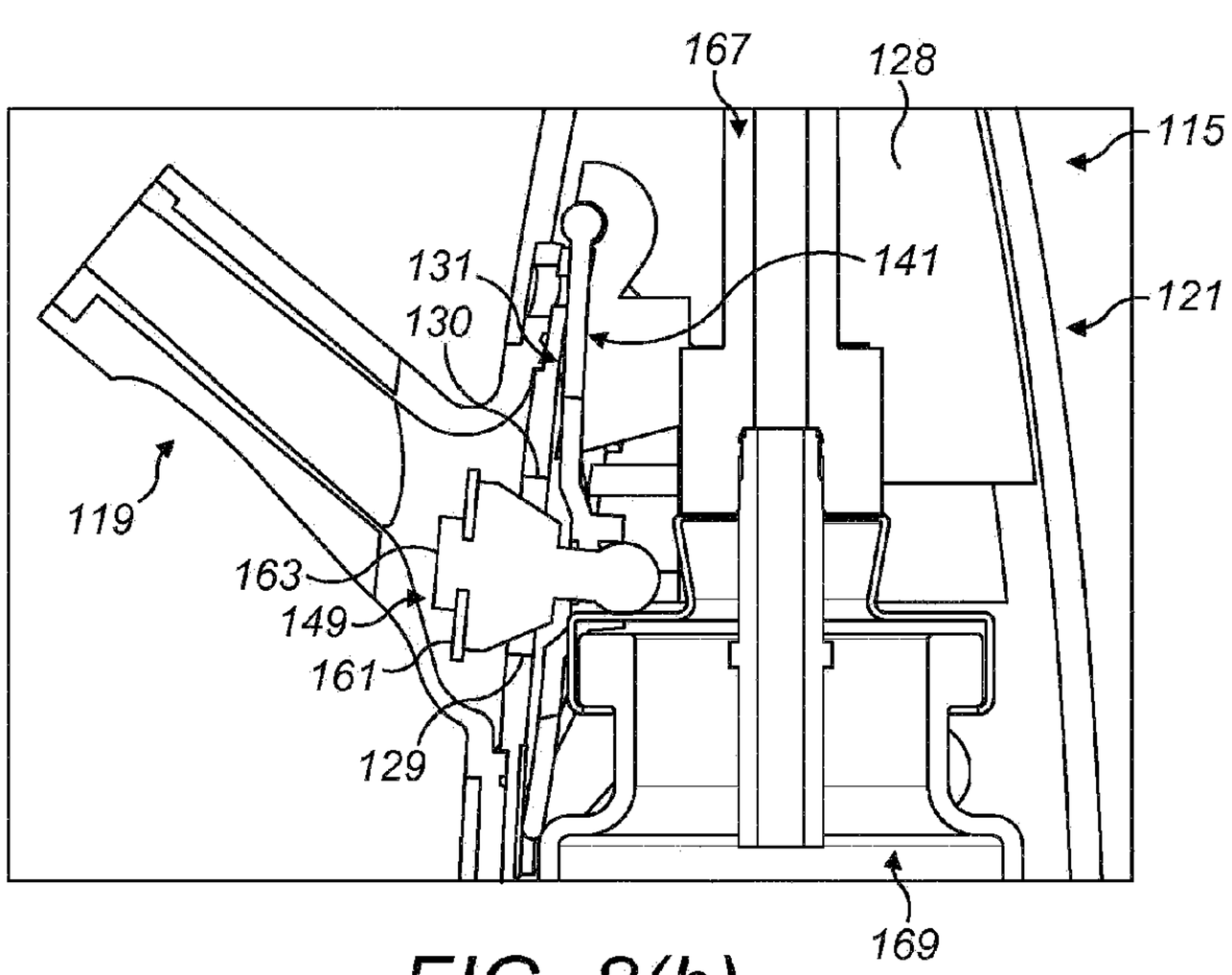

167
128
115
131
141
130
121
119
163
149
161
129
169

FIG. 8(a)


167
128
115
131
141
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121
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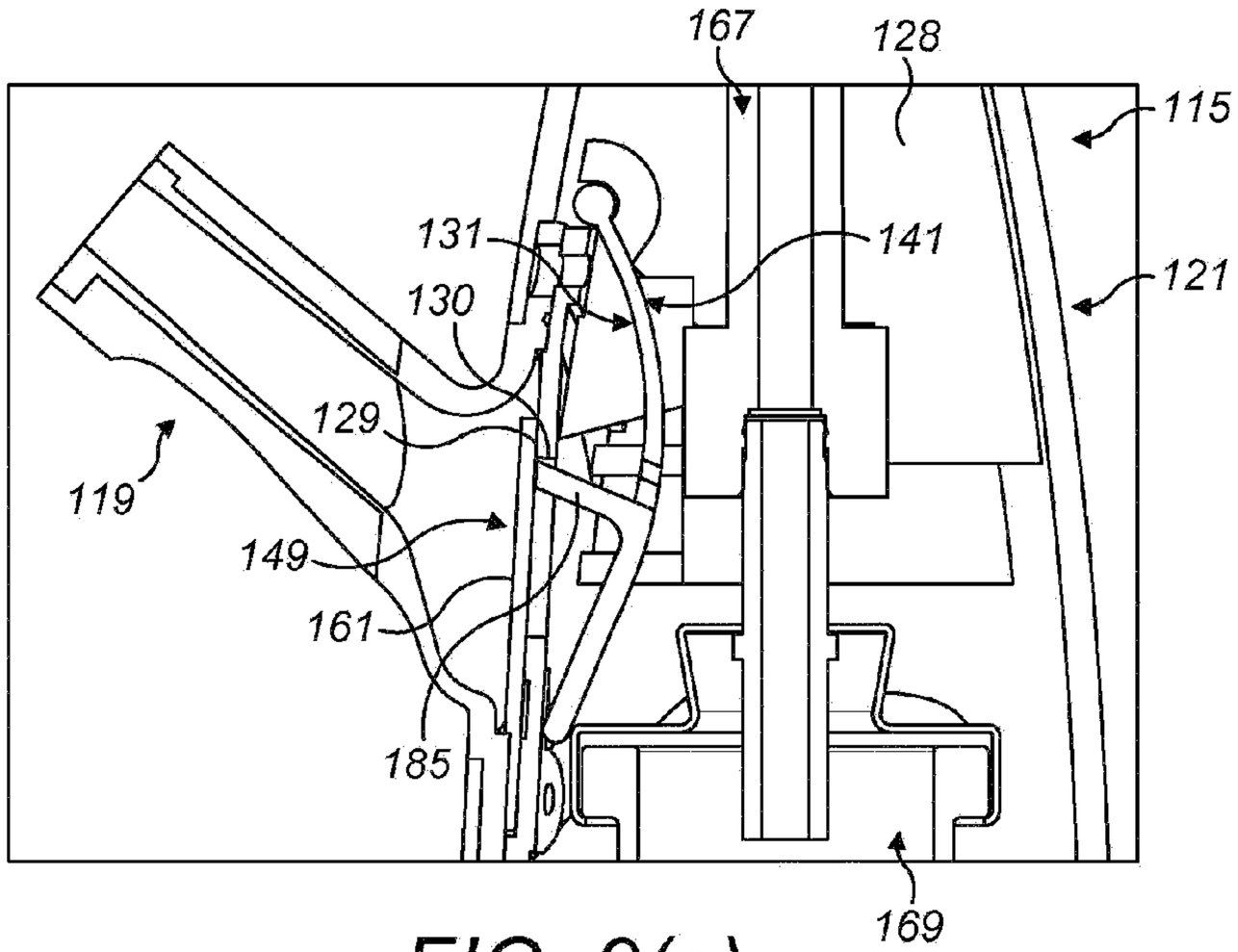
163
149
161
129
169

FIG. 8(b)


167
128
115
131
141
130
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129
119
149
161
185
169

FIG. 9(a)

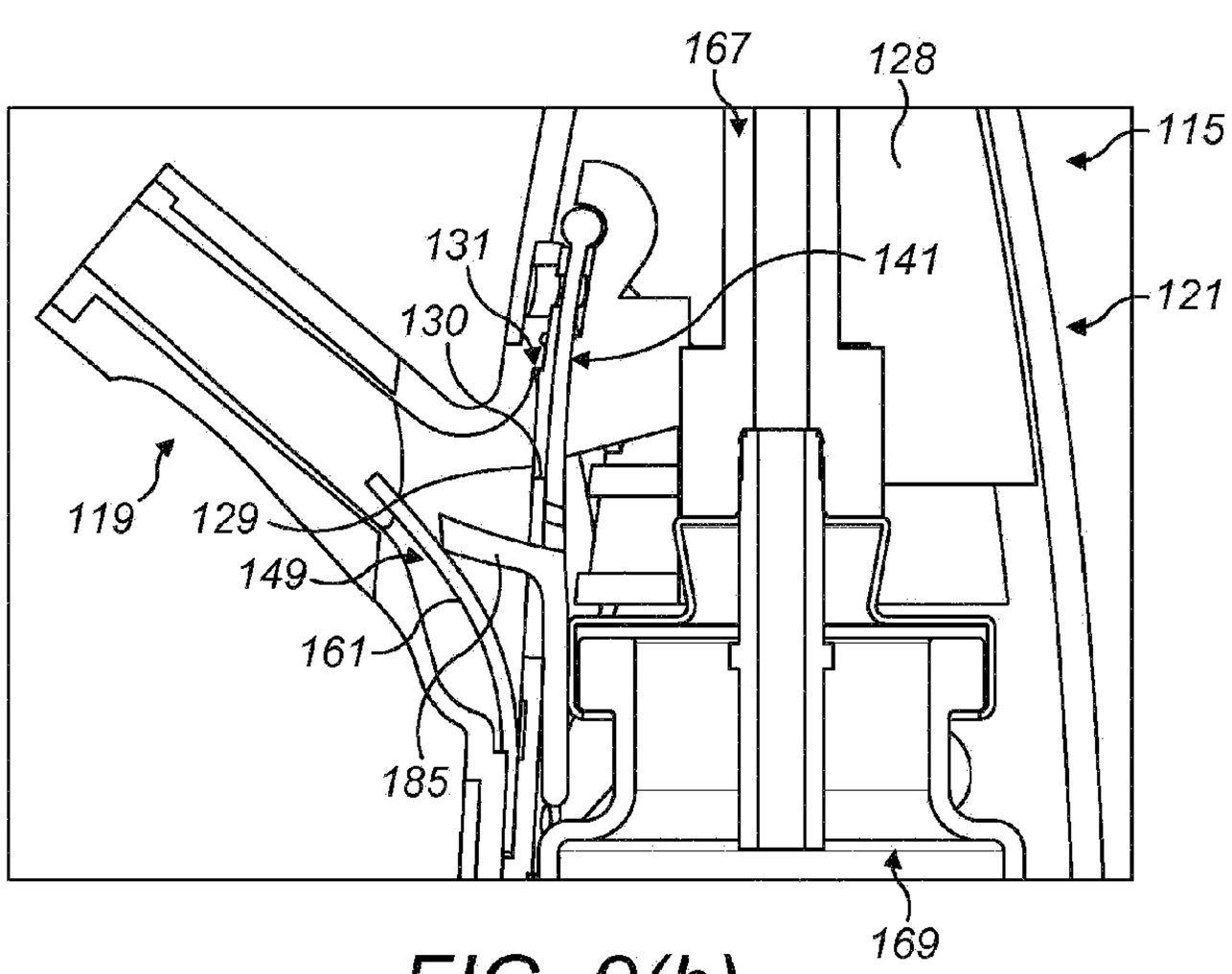
167
128
115
131
141
130
121
119
129
149
161
185
169

FIG. 9(b)

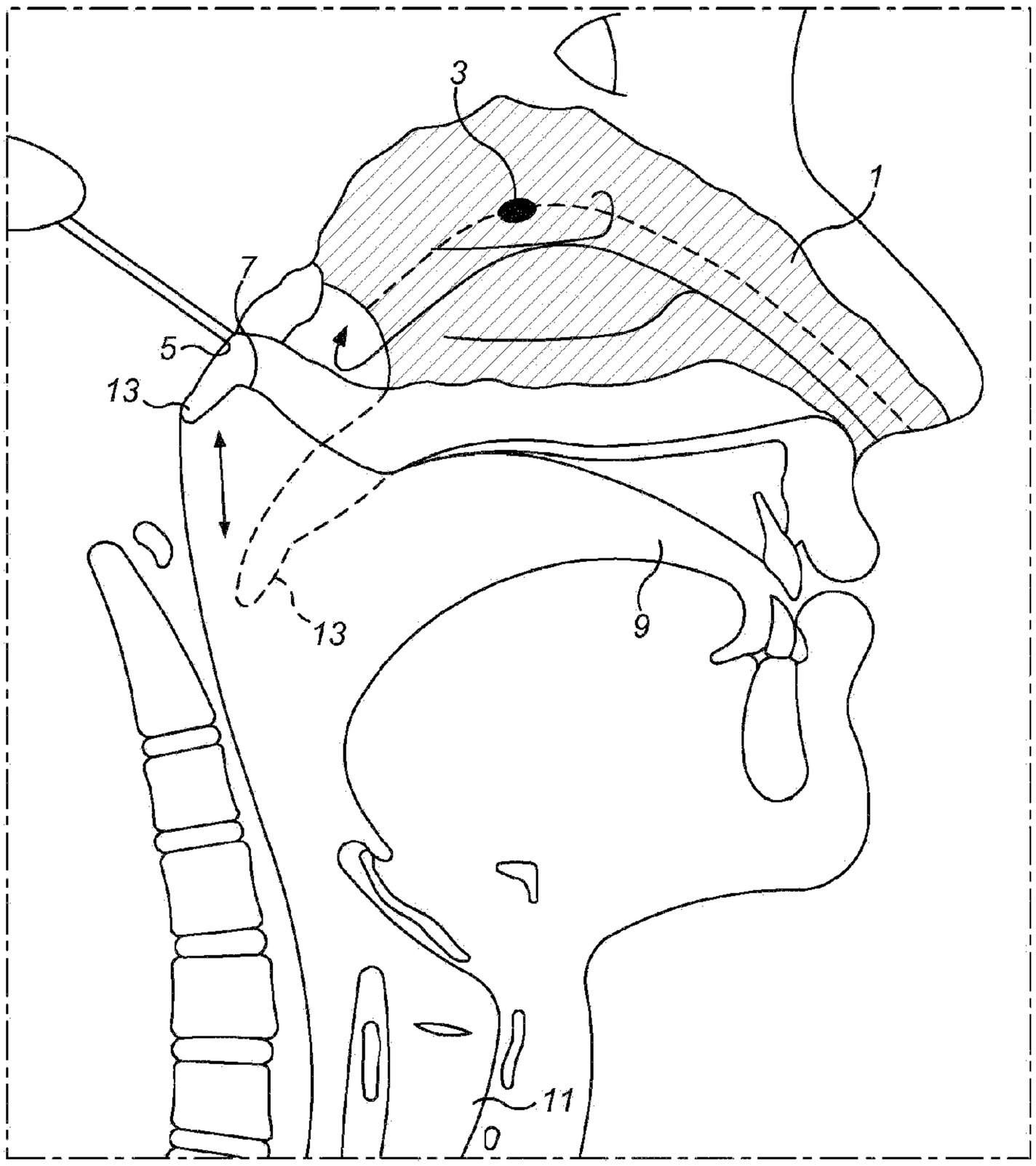

FIG. 10